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## EFECTROPHYSIOLOGICAL MEASUREMENT OF HUMAN AUDITORY FUNCTION

bу

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#### ELECTROPHYSIOLOGICAL MEASUREMENT OF HUMAN AUDITORY FUNCTION

As its title directs, this essay will deal with people, with the sounds they hear, and with the bioelectrical activity those sounds generate. While it will emphasize the way sounds influence man's brain waves, these brain waves are only one of many electrophysiological events which signal his responsivity to sounds. Every sound one hears can activate, in theory at least, every nerve and muscle in the body, and each of these structures can generate an electrical current which appropriate amplifying and recording instruments will make visible for inspection.

Consider for instance a loud noise that makes a person jump, and suppose him to have several electrodes attached to his skin (of head, arms, etc.) which are then connected to amplifiers, oscilloscopes, etc. The jump, or startle response, denotes a synchronized contraction of arm and leg muscles, a synchrony which is also precisely revealed in the pattern of electrical discharges those muscles emit. A muscle response may be so small that little actual movement is seen but its electrophysiological output is likely to be recordable nevertheless. The muscles responsible for the eyeblink can be recorded in this way (11) as can even those few vestigial human remains of the muscles that twitch the ear in animals like the cat (3).

Such electrophysiological measurements also reveal soundinduced activity in the muscles and glands controlled by the autonomic
nervous system. Thus, in infants wired for recording of the

electrocardiogram, tones of only moderate intensity will regularly alter their heart rate; this heart-rate response has been effectively put to work as a way to test their hearing (29). In adults, and under certain conditions, audible tones cause sweat glands to put out more of their product and hence measurably change the resistance to a current flowing between electrodes on the skin; this response, too, has been employed as a hearing test, although if often turns out merely to produce an unwanted artifact in certain experimental situations (24).

## Electrical Responses of the Brain

While the above examples show sounds to influence a very wide range of body functions, the one most often studied by electrophysiological methods is that of the brain itself. Its ongoing electrical activities are delicately sensitive to alteration by sound inputs, as the following three instances will illustrate.

The EEG. The human brain is unique among our body tissues in the spectrum, amplitude and variability of the electrical waves it generates. These brain waves (the EEG), large in size and easily recordable with modern methods, present to auditory physiologists and clinicians robust phenomena for study. The effort to modify these EEG waves by speech, noise and tones has a long and interesting history which deserves far more space than can be devoted to it here.

As an example of an early study in this direction, my colleagues

and I once tried to establish the threshold of hearing by examining the faintest sound which would produce a reliable change in the ongoing brain wave record (23). In those precomputer days we could state only that a weak tone at about the level of hearing threshold might alter the EEG in several ways: if the record was dominated by waves of a given frequency a sound could speed them up or slow them down, and/or cause a large deflection (an evoked response) to appear. Despite the primitiveness of this "eyeball" method of LEG analysis, however, a reasonable estimate of hearing could often be established in this way.

A sophisticated variant on this theme used computers to analyze the brain wave activities in 200 astronaut candidates (40). This study reports normative data on the EEG during sleep, quiet wakefulness and extreme focusing of attention. It established what EEG frequencies were present at each of 18 scalp electrodes and then compared these with one another to yield data on shared frequencies, their amplitudes and their phase relations. These spectral lensity computations were then repeated while the astronaut candidates performed in a variety of visual, somesthetic and auditory tasks. When attending vigilantly to a pattern of tones the men produced EEG patterns distinctly different from those seen when they performed in comparable visual tasks. The authors argue that such changes in EEG patterning, if continuously monitored, could warn interested parties (such as the astronauts themselves) of defective attention to, and processing of, messages arriving by ear.

The CNV. In addition to its EEG waves, the brain also creates and maintains standing potential differences between any two points on its surface. Electrodes applied to the scalp can see these potential differences and show the way they vary in size with the passage of time. Excellent reviews (15, 19) describe these variations - the so-called "contingent negative variations" (CNV) - and relate them to important sensory, motor and intellectual activities in man. Stutterers, for instance, systematically generate different CNV responses than do normal speakers (43).

Sound stimuli are frequently used in clinical and laboratory situations where CNVs are first initiated and then reduced in size. The main aim of these studies, however, is to relate CNV presence and amplitude to a variety of perceptual, motor and cognitive acts for which the question of whether it is a sound that evokes or abolishes the CNV is a matter of secondary importance. Nevertheless, the CNV can be sound-produced, and hence deserves at least this brief mention here.

The Auditory Evoked Response. The third type of brain response to be considered here is called the evoked response. These are electrical wave-sequences time-locked to a stimulus; they appear because the nerve activity initiated by a stimulus invades the nervous system in an orderly way.

In Figure 1 an artist has located man's auditory nervous system within his head. Any sound striking the ear will activate brain cells in the particular sequence and order shown in the left lower part of

the figure. If that sound were to be an abrupt event - a hand clap, say - it would generate electrical potential changes within each named collection of brain cells like those shown on the right of the Figure. The characteristics of these locally evoked potentials - their latency, amplitude and waveshape - have of course been best worked out in animals since such a study requires that the recording probes be exactly placed within each of the anatomical structures in question. Even though the direct information comes mainly from animals, however, there can be little doubt that what holds for them holds also for man: 1) each cell collection, or nucleus, that makes up the human auditory pathway of Figure 1 generates electrical current when sound strikes the ear, and 2) the farther from the ear, the larger the time before the structure in question begins to produce its current.

Detecting these sound-induced electrical currents has become fairly routine during the past 10 years, thanks to computer averaging techniques. One first pastes standard electrodes to a person's scalp, delivers sound stimuli to his ear or ears, and then amplifies the brain waves in the conventional manner. If the sound is a click delivered through earphones, and the subject's brain responses to perhaps 1000 of these clicks are computer-processed, recordings like that of Figure 2 result.

In each section of Figure 2 the moment the clicks were delivered appears at the left. The top section reveals the waves that appear during the first 10 milliseconds after this click-delivery: seven

of them for counting and labelling. The middle section extends the time base to 50 msec, and the bottom one to 500 msec; each of these sections demonstrates the accrual of new waves, progressively later in time, until a total of 15 can be counted during the interval of one-half second following delivery of the click. This entire collection of 15 waves is known as the human auditory evoked response.

This evoked response to an auditory signal is obviously a complex electrical event. It reflects in some way the progressive and orderly spread of the effects of stimulation through the auditory pathway depicted in Figure 1, and then from one region of the cortex to another. Which structure generates which wave is an important but largely unanswered question. The wave labelled I almost certainly reflects activity in the auditory nerve, and hence indexes the first neural event in the human auditory pathway. The later waves in the roman numeral sequence (II-VI) represent the progressive activation of the brainstem portions of the pathway up to about the inferior colliculus level of Figure 1, but the exact relationship between a given wave and its initiating structure(s) is far from clear. Studies underway using patients with various lesions in the brainstem should help to clarify these relationships (34, 37).

The middle latency (10-50 msec) responses of Figure 2, though in the past a subject of controversy, can clearly be shown to originate in the brain, not in movements of the eyeball or from contractions of scalp muscles (26). It seems probable, however, that they reflect activity not of the specific auditory cortex, but of the areas to which

it projects (cortex?, thalamus?). Intensive efforts to quantify and apply these responses to the diagnosis of hearing disorders are under way (21).

The timing of the late waves of Figure 2 (N<sub>1</sub>-P<sub>2</sub>-N<sub>2</sub>) is such that they must originate within structures to which the auditory pathway of Figure 1 projects. Direct measurements in man on the operating table suggest a latency of 12-15 msec for arrival, and perhaps 60 msec for completion of the specific auditory cortex activity initiated by a click delivered to the ear (4). (These auditory cortical events, incidentally, are apparently invisible to electrodes at the scalp). All the waves with latencies beyond about 60 msec or so must come, therefore, either from structures invaded by nerve fibers that originate in the auditory cortex and move the message from there to more distant regions, or by way of reticular pathways outside the classical one shown in Figure 1.

The difficulty in precisely assigning anatomical origins for these various evoked response waves is worth summarizing. The waves themselves are simply the voltage differences developed over time between two conductors attached to the head. The wave sequence gives only the moment-by-moment algebraic sum of all such currents generated within the brain, currents which then flow through it, the skull and the skin to reach the recording sites. The total number of these generators of brain current is unknown but large. A physicist might therefore consider this to be the problem of a 3 dimensional volume conductor within which numerous source generators (those of Figure 1,

plus others) drive electrical currents of varied onset, amplitude and duration along unknown paths of unknown impedance, and in the face of this complexity consider any effort to make an analysis of the problem hardly worth his time and effort. Many physiologists agree that these scalp recordings of brain activity are exceedingly unattractive for analysis, and they turn instead to the far more precise microelectrode techniques. What is to follow, however, argues that the study of these gross surface electrical phenomena has led to some surprisingly interesting findings and conclusions. As we shall see, the early group of waves (1-10 msec) reflect certain physical aspects of the sound stimulus with such gratifying accuracy that they can be used for testing hearing in the clinic, while the late waves (100-1000 msec) offer us a glimpse of the brain doing some of its most important work.

# The Brainstem Evoked Responses

Ten years ago the responses shown in the top section of Figure 2 were unknown. Our present knowledge of it began in 1967 with almost simultaneous reports from Israel, France and Japan. In that year, and with the help of the newly developed computer techniques, the first wave in the series (wave I) was identified by Sohmer and Finemesser (32) using scalp electrodes, and by the Portmann and Yoshii groups (27, 42) using an electrode in the ear canal. These discoveries made direct electrophysiological measures of auditory nerve activity in man practical for the first time. The Yoshii-Portmann method yields what is now called the electrocochleogram widely used as a clinical test for

hearing (see 6 for a recent summary and bibliography on this topic). The method pioneered by the Sohmer group yields the brainstem evoked response, or BER.

The first description of the BER wave sequence in its entirety, as well as many details on how it varies with changes in the auditory stimulus provoking it, was provided by Jewett and Williston in 1971 (16). During the past several years my colleagues, and I have been studying this BER. Our efforts, which will be emphasized in the following account, typify those under way in other laboratories also.

Sample normal BERs can be seen in Figure's 3 and 4. Each tracing there is the physiological response recorded between electrodes at the top of the head (vertex) and behind the stimulated ear (on the mastoid bone). Since these responses are of small amplitude (see calibration), high amplification (x 10<sup>5</sup> or 10<sup>6</sup>) and repeated stimulation (2-4000 clicks at a rate of 30 per sec) with computer averaging were required. In our laboratory two or more such responses are regularly superimposed, as in this figure, to permit estimation of response reliability.

The outstanding properties of the BER can be enumerated as follows.

- 1) No waves are present for clicks too weak to be heard, and wave V-the most prominent and stable member of the collection can usually be identified at 5 or 10 dB above an adult listener's threshold.
- 2) As stimulus intensity rises so too does response amplitude; in addition, the response latency (i.e. the interval between eardrum

movement and the peak of a given response wave) shortens. This inverse relationship between stimulus strength and wave V latency is highly reliable within and across subjects regardless of age (newborn to 75 years) or whether they are asleep, awake or unconscious (1, 9, 12, 13, 16, 26, 30, 37, 39).

- 3) Tone and noise bursts also evoke the BER. With such stimuli one can demonstrate the cochlear microphonic component of the auditory evoked response (39) as well as the fact that the steepness of stimulus rise-time is the critical factor for evoking the BER (14). Appropriate noise masking experiments have, furthermore, identified the nerve fibers arising in the base, or high-frequency, portion of the cochlea as the ones that are stimulated to produce the response (12).
- 4) The use of tone stimuli has also uncovered a second type of brainstem response, the so-called frequency-following response (FFR). First reported in 1973 by Moushegian et al (22), the FFR is a sinusoid generated in the brain stem to tones below 2kHz (18, 20). Like the BER which appears along with the FFR the FFR is a small voltage that requires computer averaging for its demonstration. Its discovery opens new but still largely unexplored avenue for electrophysiological investigation of the human auditory system.

Several attempts to use the BER (and the FFR) to answer questions of theoretical and practical interest can be outlined here. In hearing clinics, the BER permits an estimate of hearing threshold in patients such as newborn infants where other methods yield equivocal

answers or none at all (9, 17, 30). It is also clear that persons with hearing loss due to impaired conduction of sound waves to the cochlea (conductive loss) can produce abnormal BERS that differ from the abnormal ones generated by patients whose deafness is due to damaged cochlear hair cells (sensory neural loss: 9). The clinical use of the BER, finally is not limited to audiology; it apparently has rich potentialities as a general neurological tool also. Because tumors, trauma and demyelinating diseases can interrupt the brainstem auditory pathways at many different levels, a lesion at a particular level can be expected to alter the BER wave-pattern in characteristic ways; recent evidence indicates this idea is correct, at least in principle (9, 33, 37).

In the small number of laboratory studies so far reported, the BER produced by a given signal has remained constant regardless of stage of sleep (1) or state of attention (25). When the apparent loudness of such a signal is enhanced by special techniques, no change in the BER takes place (2), but it does reflect by a drop in its amplitude the temporary shift in threshold that follows exposure to loud sounds (34). This small sample of studies will doubtless be followed by many more in which the BER (and FFR) is examined in monaural and binaural listening situations of interest to psycoacousticians (e.g. masking, binaural localization and loudness and frequency discrimination). Such developments are almost inevitable since this new method is relatively simple to apply and the data it yields are stable, objective and highly sensitive to changes in the acoustic

stimulus parameters.

The late waves of the human auditory evoked response are those labelled N<sub>1</sub>-P<sub>2</sub>-N<sub>2</sub> in the bottom mection of Figure 2. Unlike the BER, which as we have just seen behaves as if it were physiological sound-level meter, these late waves tend instead to reflect the ups and downs in the way an individual deals with the sounds he hears. For instance, deep sleep, which has no influence on the BER, dramatically changes the amplitude and latency of the N<sub>2</sub> wave. To varying degrees, the several late waves seem to reflect not so much the physical features of the sound that strikes the ear as what goes on within the head as a listener assigns "meaning" or "significance" to an auditory stimulus. A study recently reported from our laboratory (25, 26) will illustrate this point.

Suppose we present about a thousand clicks (at a rate of around 1 per sec) to a subject wearing earphones, and record the responses they evoke. Suppose, further, that about 10% of the clicks are weak ones randomly introduced into the train. Finally, suppose that the subject hears these strong and weak clicks under two conditions: 1) he is instructed to pay no attention and to read an interesting book ("Ignore"), and 2) his task is to count each weak click and report the total correctly at the end of the run ("Attend").

Figure 5 shows representative results presented in the format of Figure 2. Signif.cant differences between the two columns of Figure 5 appear only in the late waves, where the  $N_1$ - $P_2$  deflections are clearly larger in the "Attend" recordings. These differences are reasonable stable, furthermore, since four replications of the experiments nicely superimpose. One may conclude, therefore, that "attention", as defined in this case, is revealed by an increase in  $N_1$ - $P_2$  amplitude. Several experiments of this type from our laboratory (31) and elsewhere (5, 28, 35) yield the same overall conclusion.

The responses shown in Figure 5 were extracted from the EEG following delivery of the louder (90%) clicks in the train. Figure 6 shows the late waves evoked by the weaker (10%) members of the train, and at 3 different points on the head ranging from front (Fz) to back (Pz) in the midline. These responses can be expected to reflect, then, any peculiar brain events associated with the special targets of the listener's attention.

Two major differences between the left and right columns of Figure 6 are apparent. In the "Ignore" condition  $N_1$ - $P_2$  is everywhere present but very small, because the target click was weak. In the "Attend" state  $N_1$ - $P_2$  is everywhere larger, which we have just learned is what should happen. But this  $N_1$ - $P_2$  change is trivial compared to the impressive downward-going wave unique to the "Attend" recordings. It is a positive wave with onset at around 300 msec post-stimulus and a duration of several hundred msec. It belongs to a group of such late positive waves discovered 10 years ago (5, 38) to which the name  $P_3$  (or  $P_{300}$ ) has been assigned.

This unique association of a P3 wave with attention to a

nothing at all. This situation was simply accomplished by occasionally omitting a click from the regularly repeating train of them, the subject's task being to count the missing clicks and report, as before, the total number. Figure 7 shows the huge P<sub>3</sub> subjects generate when, as in this case, their target is no stimulus whatsoever.

The  $P_3$  of Figure 7 means that this wave indexes wholly endogeneus brain events, processes that go on exclusively inside the skull. Here  $P_3$  is an electrical sign of whatever goes on inside the brain when a target has been identified. Since it is a brain wave invariably associated with perception of a sound not delivered, it must be a sign of the perception itself.

vealed by the P<sub>3</sub> of Figure 7 indexes the same brain processes revealed by the P<sub>3</sub> of Figure 6 - as many believe - one can conclude that a purely subjective event has been under way whenever a P<sub>3</sub> is recorded. In a recent review (36) my colleagues examined 19 P<sub>3</sub> papers by 43 authors and concluded that P<sub>3</sub> appears, or is enhanced - at the time a signal is detected; when one signal is deemed to be different from another; when a guess is confirmed or disconfirmed; and when a signal means "shift to a different task". In short, P<sub>3</sub> does seem to reveal when a subject has been importantly engaged in a conscious process: it says he has been aware, gotten the message, made up his mind. No other electrophysiological response taps so directly these important aspects of our everyday behavior.

Many laboratories are presently working with these late waves

which vary with cognitive processing of acoustic signals. As one example - the only one space permits - several use human speech sounds in search of hemispheric asymmetries in amplitudes and latencies of the N<sub>1</sub>-P<sub>2</sub>-P<sub>3</sub> sequence. Since the left hemisphere in most right handed persons is far more important for speech functions than is the right, some corresponding difference in the late waves is not unreasonable to expect. Both success (eg. 41) and failure (7) to demonstrate these response asymmetries have been reported to date. In this important field where so little is known and where good information would yield so much of practical value, one can hope for an early resolution of the question.

Summary. During the quarter century this volume commemorates our understanding of the human auditory evoked response has moved forward at an ever-accelerating pace. Hard won basic knowledge, helped immeasurably by the computers, has defined all its major deflections. We can state - with reasonable confidence - the way particular changes in a stimulus will be coupled to specific changes in the response, and even how a listener's state of mind will influence the response he gives.

Important practical applications of this basic knowledge have begun to appear. Evidence grows, for instance, that the brainstem portion of the response can be developed into a useful hearing test especially for infants. Hearing tests for preverbal and nonverbal children are not yet the precise instruments they should ideally be. The BER, which can state unequivocally now well the peripheral auditory

apparatus functions, would be a welcome addition to the clinician's armementarium.

Clinical applications of the waves evoked at alout 100 msec and later await the development of still more facts. These waves are clearly related to brain events associated with cognitive processing of acoustic signals since their properties depend upon where the listener directs his attention, whether the signal is an expected event or a surprise, and when a sound that is listened-for is heard at last. Unfortunately, the details of what is going on are still somewhat vague, and most of the specific rules that pertain remain to be clarified.

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#### FIGURE LEGENDS

- Fig. 1 The human auditory pathway shown in place (upper left) and isolated (lower left). Electrical waves that would be aroused by a click in each station of the pathway are diagrammed on the right.
- Fig. 2 Components of the human auditory evoked response. Each trace shows the average of 1024 responses to clicks (60 dBSL) delivered at 1 per sec to the right ear. Electrodes: vertex (positive up) to right mastoid. Responses shown were extracted from tape-recorded EEG by an average response computer (Fabritek 1052) at different gain and on 3 different time bases. (From 26).
- Fig. 3 The brainstem response (BER) evoked from a normal-hearing young adult. Electrodes: vertex (positive down) to mastoid.

  Each trace sums 2000 responses to monaural clicks (30 per sec).

  Note wave V latency increase as signal strength (dBSL) decreases. (From 9)
- Fig. 4 The BER from infants and children recorded under conditions like those of Fig. 3. All stimuli at adult 60 dBSL level.

  Note wave V latency decrease as children grow. (From 12).

- Fig. 5 Effect of attention on the human auditory evoked response.

  Details as in Fig. 2. Attend: subject counted an occasional faint click (32 in all) interspersed among 992 louder ones.

  Ignore: The same clicks were presented while the subject read an interesting book. Only responses to the louder (60 dBSL) clicks appear here.
- Fig. 6 Details as in Fig. 5. Responses to the 32 weak clicks are shown here, on the long time base and at 3 different scalp locations.
- Fig. 7 Records from an experiment like that of Figure 5 except that the faint click was simply omitted. Interclick interval 1.1 sec; computer was triggered by the click preceding the omitted one. Each trace shows average of 64 responses (Fig. 5, 6, 7 from 25).

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